3198

Histological changes produced by inversion of nipple flaps of mammary gland of the rabbit.*

WILLIAM H. HARRIS.

[*From the Department of Pathology of the Tulane University School of Medicine, New Orleans, La.*]

Inverted and bleeding nipples and chronic inflammatory lesions of the human breast are frequently noted as forerunners of cancer of this structure. These conditions often present the aspect of the "indifferent vorstadium" described by Ribbert[1] or the picture commonly alluded to as the so-called precancerous stage.

The experiments herein noted were performed with the view of ascertaining what results would follow the inversion of nipple flaps in the mammary gland of the female rabbit.

Eight female rabbits purchased in the open market were employed and their histories and ages are therefore not known. Two of these rabbits were lactating and one other was not full grown. Twenty-eight operations were performed. Eighteen different nipple flaps were inverted and ten of the nodular masses thus produced were bisected and reinverted in other areas. The operations, as a whole, consisted in cutting a rectangular flap in which the nipple was included and the basal attachment of the flap was not disturbed, thus maintaining the circulation from that source. The depth of the flap extended down to the areolar tissue, thus including the skin and gland structure beneath. It may be mentioned that in the quiescent breast, the gland of the rabbit is rather rudimentary in its gross aspect; where lactation is present the gland is well developed and it was sectioned completely through in order to procure the flap. The tip of the nipple was clipped off and the stump cross sectioned and scraped. The underlying gland was also scraped and partially sectioned. The flap thus prepared was inverted with the nipple downward and then drawn beneath the overlying structures by means of a retaining suture. When the inverted flap was in the vicinity of the

* Aided by a grant from the B. M. Harrod Cancer Research Fund.

[1] Ribbert, "Geschwulstlehre," Boun, 1904 or *Aertz. Sach. Zeit.*, 1898, 389, cited in "Neoplastic Diseases," Jas. Ewing, 1922, p. 993.

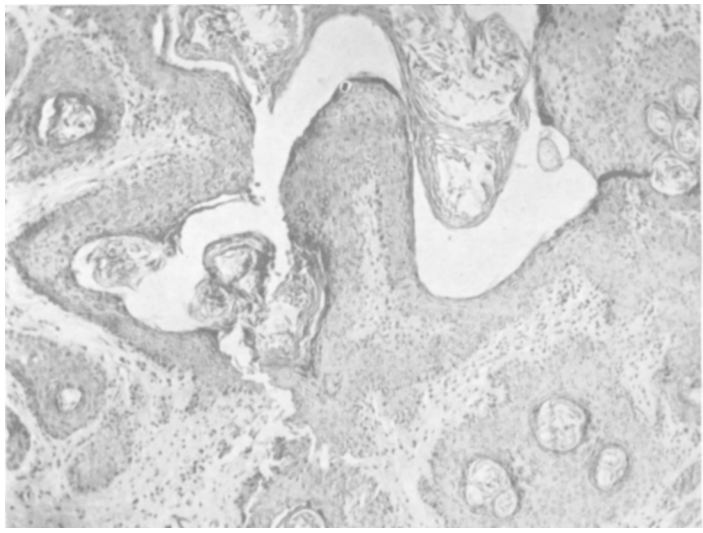

FIG. 1.

Papillary protrusions and epithelial cell multiplication about hair shafts and occurring in skin epithelium of inverted flap.

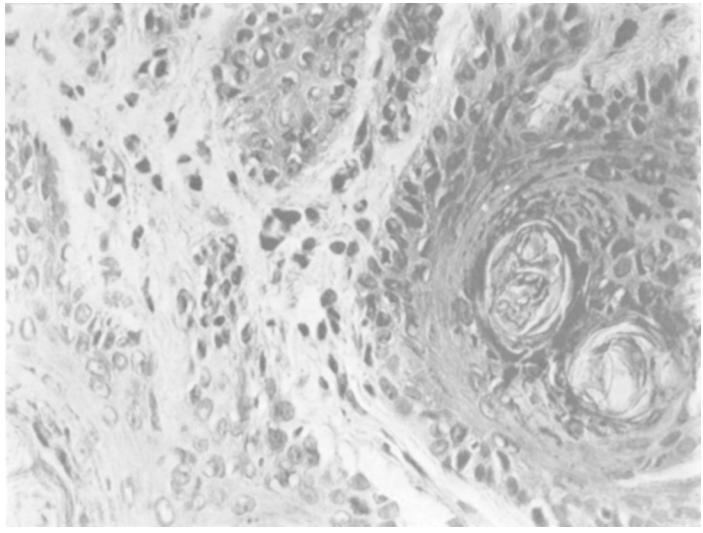

FIG. 2.

High power area corresponding to Fig. 1 showing rapidly growing epithelium with mitotic figures.

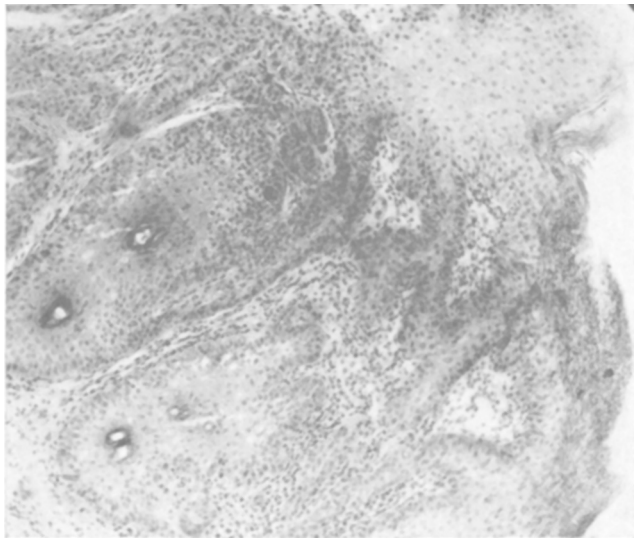

FIG. 3.

Section of inverted flap after 4 weeks standing, presenting extensive proliferation of squamous epithelium of hair shafts and surface with downward extension of skin epithelium, simulating epithelioma.

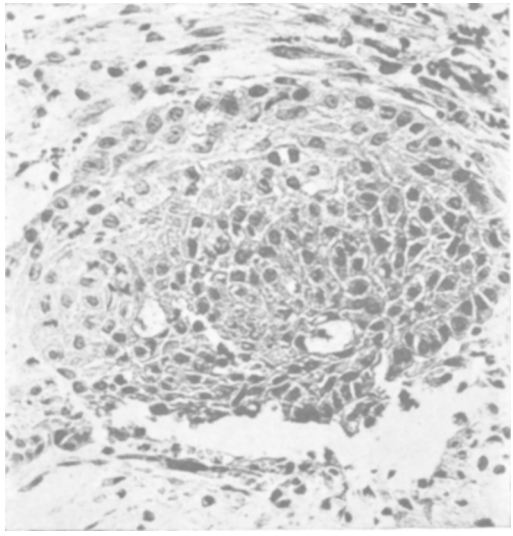

FIG. 4.

Island of prickle or spine cells located deep beneath the surface epithelium. Many mitotic figures are present.

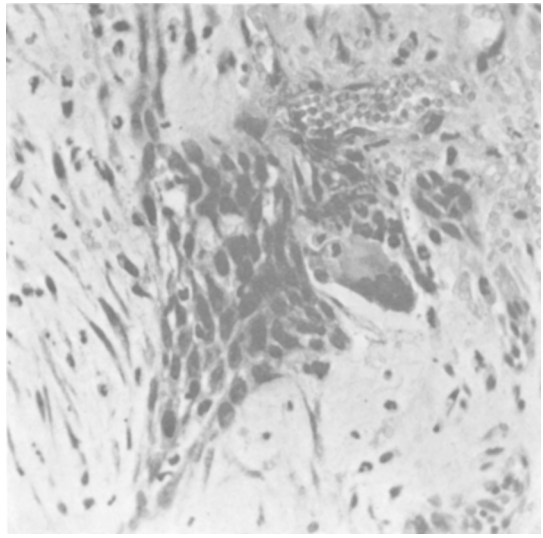

FIG. 5.

An isolated strand of skin epithelium demonstrating organization by fibroblastic cells with the presence of scattered polymorphonuclear leucocytes and a foreign body giant cell; all of which are processes of extinction of the growing epithelium.

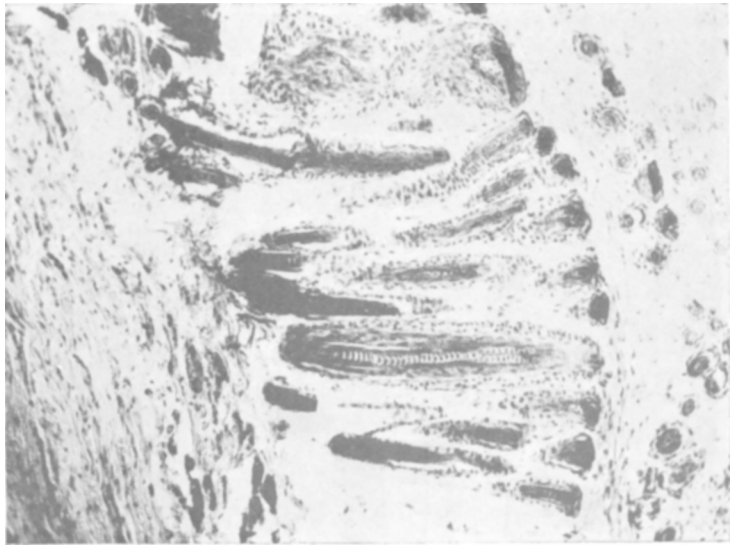

FIG. 6.

Hair growing downward from the inverted flap. This growth often attained an inch or more in length.

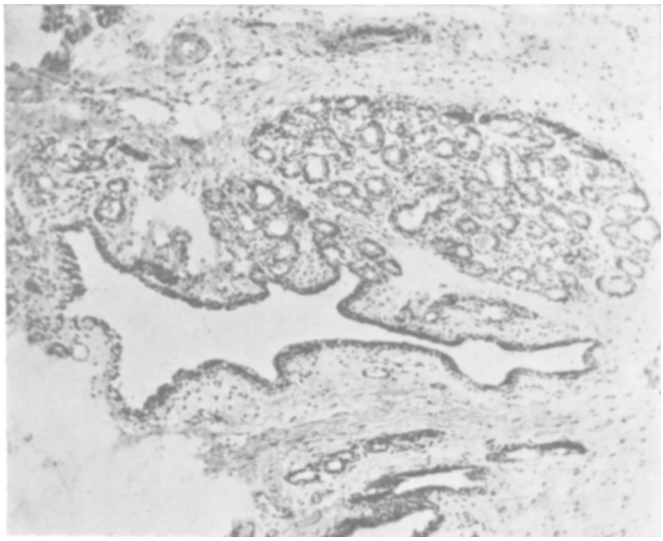

FIG. 7.

Inverted mammary gland structure persistent and well preserved after one month.

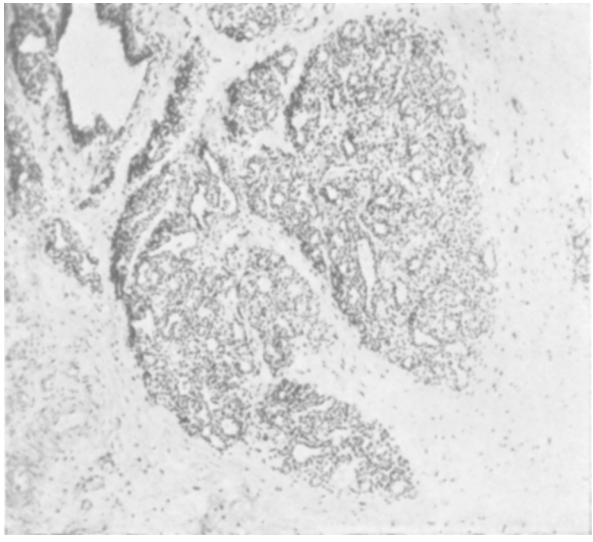

FIG. 8.

Ducts of mammary gland showing aberrant growth of epithelium after inversion for 6 weeks.

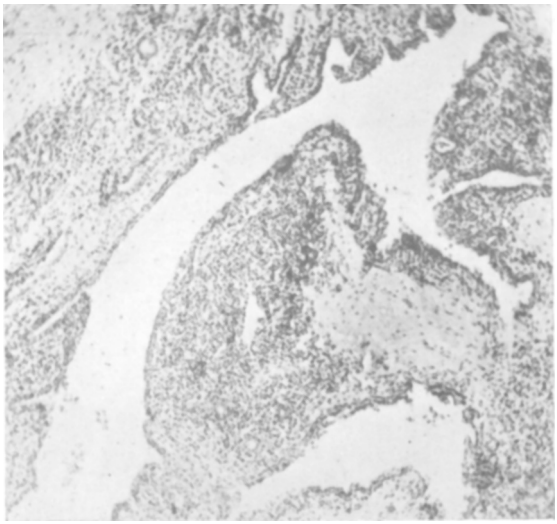

FIG. 9.

Intracanalicular papillary protrusion covered with multiple layers of epithelium occurring in the inverted mammary gland flap.

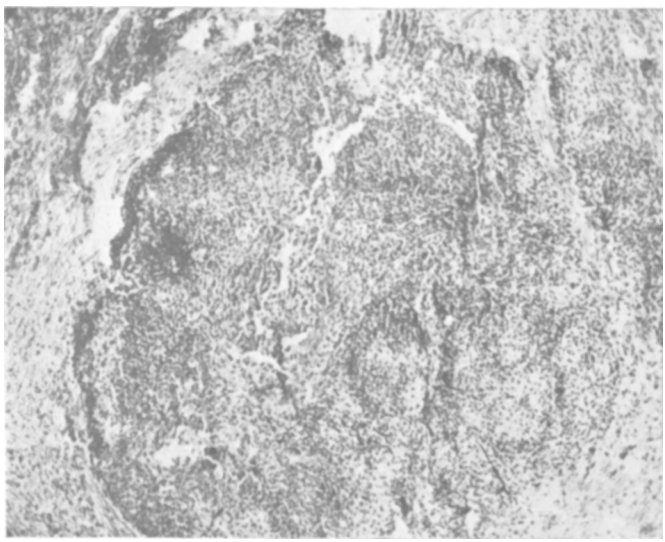

FIG. 10.

Massive irregular growth of epithelium derived from the gland structure, simulating carcinoma in aspect. Flap inversion is of eight weeks standing.

pectoral muscle it was imbedded beneath this structure and retained there by a suture. The gaping wound remaining was sutured lightly together so as not to severely embarrass the circulation at the base and a sterile dressing was applied. The operations and observations have extended over a period of seven months.

As a result of this operative procedure, reactionary nodules were formed in all instances. Acute inflammatory evidences were present primarily both grossly and microscopically about the inverted flap. The congestion and edema subsided after two weeks but nodulation persisted. Study was directed especially towards the action of the epithelial cells placed under these abnormal conditions. It is of interest to note that greater activity was observed on the part of the skin epithelium of the inverted flap than for that of the gland cells. This fact is probably due to the greater proliferative tendency of skin epithelium, and also because its misplacement was more abnormal than that of the gland cells. Portions of the nodules that were formed were removed at various periods of time such as after the first, second, third, fourth, fifth, sixth, seventh and eighth weeks. In the microscopic study of the sections it was found that the inverted gland epithelium persisted in duct formation for four or five weeks. In certain nodules the cells grew at random from the confines of the basement membrane and the tubular arrangement was lost or only poorly shown in certain areas. It is noteworthy, however, that these cells did not assume the distinctly modified aspect found in cancer cells, *i. e.*, their general morphology and tinctorial property adhered rather closely to the original cell type. In the instance of the epithelium of the skin and hair shafts, however, the cells were frequently of a more aberrant type. Often appearances analagous to those of the basal and spine-celled epitheliomata could be found. The epithelial cells of the hair shafts were especially active in their proliferation and mitosis could be noted. In some nodules continued growth of the hair shaft in an inverted manner was found. At times there were present cystic masses containing sebaceous matter and hair resembling in aspect a dermoid cyst. Enlargement of the adjacent lymphatic glands was frequently noted and at times specimens were removed for examination. They were found to present, microscopically, chronic proliferative adenitis, probably the results of absorption of cell products.

Of special note were the defensive methods presented by the host, preventing the continued aberrant growth of these misplaced epithelial cells. Primarily, the inflammatory cells, through their activity, produced degenerative changes in the flap cells, but of greater importance was the connective tissue response which seemed to form the main defensive barrier, not only surrounding and barricading the cell growth, and curtailing its blood supply, but actually invading and organizing the mass. The fibroblastic cells arose from all sides and appeared to actually crush out of existence the threatened continued epithelial growth. Occasionally, giant cells of the foreign body type appeared as destroying factors. The microphotographs illustrate a variety of the histological changes observed.

Although the nodules thus far studied appeared at times to thrive, and attained in part the appearance of malignant growth, the eventual outcome, as a whole, was degeneration and fibrosis. However, three animals with persistent nodules are still under observation.

The failure of formation of true epithelial neoplasms in these experiments appear attributable, not to the lack of impetus or inherent cell proclivity of the invading epithelium but rather to the inhibitory or restraining influences put into action by the defensive factors of the host. It is known that some species of animals demonstrate a natural resistance to epithelial neoplasm, especially for certain anatomical areas. It is not unlikely that such factors of resistance prevail to a great extent in the mammary gland of the rabbit.

3199

Evidence limiting the time of inception of intrauterine digital amputations.

HAROLD CUMMINS.

[*From the Department of Anatomy of the Tulane University School of Medicine, New Orleans, La.*]

Evidence is derived from epidermal ridge configurations, in four subjects admitting diagnosis of congenital amputations (as opposed to agenesia), which points to the existence of the affec-